

## LONG-TERM RESTRICTED INDEX SELECTION IN MICE

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### SUMMARY

Replicates of mouse lines that had been selected within full-sib families for high or low epididymal fat pad weight (EF) holding body weight (BW) constant were crossed. After two generations of random mating, two replicates were sampled to reinitiate selection for the same criteria except that individual selection was used to increase the selection differentials. Realized heritabilities for index units based on high-fat, low-fat and divergent selection were  $0.32 \pm 0.13$ ,  $0.58 \pm 0.002$  and  $0.41 \pm 0.002$ , respectively. These estimates were not significantly different from those in the first phase of selection. In both phases of selection the restricted index designed to increase EF without changing BW was in agreement with expectation. In contrast, the index designed to decrease EF without changing BW did not agree with theory since BW increased and EF remained unchanged. There was, however, some replicate heterogeneity in response, suggesting that genetic drift may have played a role.

### INTRODUCTION

Restricted index selection is expected to maximize genetic gain in the aggregate breeding value of a subset of traits while holding genetic change to zero in a second subset (Kempthorne and Nordskog, 1959). An experiment designed to test this theory and to develop divergent lines for fat content in mice involved eight generations of replicated within full-sib family selection for high or low 12-week epididymal fat pad weight (EF) holding body weight (BW) constant (Eisen, 1992). Although realized heritabilities of index units were symmetric, the correlated responses in component traits of the restricted index lines were asymmetric. Realized genetic gains in the high-fat restricted index lines were in agreement with expectation, but responses in the low-fat restricted index lines did not agree with expectations because EF did not respond downward and BW increased. The objective of the present study was to determine if low selection differentials caused by selecting within families may have accounted for the discrepant results. The approach used to try to increase selection differentials was individual selection.

### MATERIALS AND METHODS

After eight generations of within full-sib family selection, replicates of each selection treatment were crossed to each other. For the high fat replicates, HE1 (high-fat, replicate 1) was crossed to HE2 (high-fat, replicate 2) and similarly for the low-fat replicates (LF1, LF2) and control replicates (RS1, RS2). In generation 11, two new replicates consisting of 15 families each were formed in each selection treatment; these replicates were designated HE4, HE5; LE4, LE5; RS4, RS5. In the HE and LE replicates, selection was continued for a further eight generations for the same index criterion using individual selection instead of within-family selection. The restricted selection index was  $I = 11.93P_{BW} - 0.3323 P_{EF}$ , where  $P_{BW}$  and  $P_{EF}$  are phenotypic values for BW and EF, respectively. Control lines were selected randomly within families. Approximately 60 males were scored for each replicate selected line in each generation while 30 males were scored in each replicate control line in each generation.

### RESULTS AND DISCUSSION

Phenotypic statistics for the control line replicates are given in Table 1. The regressions of index units and component traits on generation number were not significant.

Phenotypic variances in I and EF and the phenotypic covariance and correlation between BW and EF were larger ( $P < 0.01$ ) in HE compared to LE (Table 2). The phenotypic variance in BW did not differ significantly between the HE and LE lines. The LE lines did not differ from the RS lines for any of these statistics (data not shown). The absolute values of the primary (index units) and secondary (EF) weighted cumulative selection differentials were larger in HE than LE (Table 3), which can be explained in part by the increased phenotypic variances in I and EF. The primary selection differentials were 74% and 25% greater in HE and LE, respectively, for individual selection (generations 11 to 19) than for within-family selection (generations 0 to 8). The realized index weights were close to expectation for all lines except HE5, where the relative weight for the trait BW was less than intended.

**Table 1.** Control line means, phenotypic standard deviations ( $\sqrt{V_p}$ ), coefficients of variation (CV) and regressions of generation means on generation number  $\pm$  standard error (b  $\pm$  SE)

Trait <sup>a</sup>	Mean <sup>b</sup>	$\sqrt{V_p}$ <sup>b</sup>	CV <sup>b</sup>	b $\pm$ SE <sup>c</sup>
I	33.7	37.99	11.27	-1.91 $\pm$ 1.21
BW, g	37.3	3.45	9.25	-0.01 $\pm$ 0.15
EF, mg	32.5	122.45	37.38	5.48 $\pm$ 5.63

<sup>a</sup> I, Index units; BW, 12-week body wt; EF, 12-week epididymal fat pad wt.

<sup>b</sup> Pooled within replicate controls (RS4, RS5) and generations 11 to 19 (n = 532).

<sup>c</sup> Pooled within replicate controls.

**Table 2.** Estimates of phenotypic statistics in selected lines for index units and component traits<sup>a</sup>

Line	Phenotypic Variance			Phenotypic	Phenotypic
	I	BW, g <sup>2</sup>	EF, mg <sup>2</sup>	Covariance (BW, EF)	Correlation (BW, EF)
HE	3,754 <sup>b</sup>	15.88 <sup>b</sup>	68,333 <sup>b</sup>	763.81 <sup>b</sup>	0.73 <sup>b</sup>
LE	1,453 <sup>c</sup>	14.32 <sup>b</sup>	14,030 <sup>c</sup>	269.24 <sup>c</sup>	0.60 <sup>c</sup>

<sup>a</sup> pooled within replicates (HE4, HE5; LE4, LE5) and generations 11 to 19 (n = 1036 for HE and n = 1032 for LE)

<sup>b,c</sup> Statistics within a column with no superscripts in common differ ( $P < 0.01$ ).

Selection responses for index units from generations 11 to 19 were symmetric (Table 4) and were larger than in the earlier generations involving within-family selection. The pooled correlated response for BW was positive ( $P < 0.05$ ) in LE and not significant in HE while the response in EF was positive ( $P < 0.05$ ) in HE and not significant in LE (Table 4). The response of epididymal fat pad weight adjusted for body weight (EFADJ) in a covariance analysis was positive ( $P < 0.01$ ) in HE and negative ( $P < 0.01$ ) in LE.

Generation means as deviations from control for all 19 generations are given in Figures 1a, b, c for I, BW and EF, respectively. For the HE selection treatment, regressions of response on generation number were  $-9.34 \pm 0.56$  ( $P < 0.01$ ),  $0.13 \pm 0.24$  ( $P > 0.05$ ) and  $32.9 \pm 10.3$  ( $P < 0.05$ ) for I, BW and EF, respectively. Comparable regressions of response on generation number

in the LE selection treatment were  $6.88 \pm 1.97$  ( $P < 0.01$ ),  $0.53 \pm 0.13$  ( $P < 0.01$ ) and  $-1.6 \pm 5.4$  ( $P > 0.05$ ) for I, BW and EF, respectively.

Pooled realized heritabilities for index units from generations 11 to 19 based on high-fat, low-fat and divergent selection were  $0.32 \pm 0.13$ ,  $0.58 \pm 0.002$  and  $0.41 \pm 0.002$ , respectively, which were not significantly different from the respective realized heritabilities of  $0.42 \pm 0.20$ ,  $0.44 \pm 0.19$  and  $0.42 \pm 0.05$  in generations 0 to 8.

Individual selection for the index yielded higher selection differentials for I and EF than the earlier study based on within family selection. However, increasing selection differentials had no

**Table 3.** Primary (index units) and secondary (BW, EF) weighted cumulative selection differentials (WCSD) and realized relative index weights (RRIW) from generations 11 to 19

Line	WCSD <sup>b</sup>			RRIW	
	I	BW, g	EF, mg	BW	EF
HE4	-280.77	5.45	1,017	31.78	-1
HE5	-292.56	8.96	1,125	24.13	-1
LE4	147.56	7.78	-166	33.60	-1
LE5	168.77	9.07	-168	36.40	-1
Intended <sup>a</sup>				35.90	-1

<sup>a</sup> Based on restricted selection index using individual selection

<sup>b</sup> Values are halved because selection was only applied to males

**Table 4.** Regression coefficient  $\pm$  SE of index units and component responses on generation number (generations 11 to 19)

Line	I	BW,g	EF,mg	EFADJ,mg <sup>c</sup>
HE4 <sup>a</sup>	$-11.72 \pm 2.70^{**}$	$-0.24 \pm 0.13$	$26.1 \pm 8.1^{**}$	$34.6 \pm 8.0^{**}$
HE5 <sup>a</sup>	$-11.67 \pm 2.70^{**}$	$0.62 \pm 0.13^{**}$	$57.5 \pm 8.1^{**}$	$31.6 \pm 8.0^{**}$
Pooled <sup>b</sup>	$-11.69 \pm 0.03^{**}$	$0.19 \pm 0.43$	$41.8 \pm 15.7^*$	$33.1 \pm 1.5^{**}$
LE4 <sup>a</sup>	$11.08 \pm 2.70^{**}$	$0.36 \pm 0.13^{**}$	$-20.4 \pm 8.1^*$	$-34.5 \pm 8.0^{**}$
LE5 <sup>a</sup>	$12.41 \pm 2.70^{**}$	$1.04 \pm 0.13^{**}$	$0.4 \pm 8.1$	$-47.5 \pm 8.0^{**}$
Pooled <sup>b</sup>	$11.75 \pm 0.67^{**}$	$0.70 \pm 0.34^*$	$-10.0 \pm 10.4$	$-41.0 \pm 6.5^{**}$
Divergence 4 <sup>a</sup>	$-22.80 \pm 2.84^{**}$	$-0.61 \pm 0.13^{**}$	$46.5 \pm 12.3^{**}$	$69.1 \pm 10.9^{**}$
Divergence 5 <sup>a</sup>	$-24.08 \pm 2.84^{**}$	$-0.42 \pm 0.13^{**}$	$57.1 \pm 12.3^{**}$	$79.1 \pm 10.9^{**}$
Pooled <sup>b</sup>	$-23.44 \pm 0.64^{**}$	$-0.51 \pm 0.09^{**}$	$51.8 \pm 5.3^{**}$	$74.1 \pm 5.0^{**}$
Asymmetry <sup>b</sup>	$0.06 \pm 0.69$	$0.89 \pm 0.77$	$31.8 \pm 36.8$	$-7.9 \pm 8.1$

\*  $P < 0.05$ , \*\*  $P < 0.01$ .

<sup>a</sup> Standard errors estimated by least-squares.

<sup>b</sup> Standard errors estimated from variance between replicates.

<sup>c</sup> Epididymal fat pad weight adjusted for body weight covariate.

effect on the asymmetry of responses in component traits. In both phases of selection, EF increased without changing BW in the HE selection treatment, and EF did not increase and BW increased in the LE selection treatment. There was, however, some heterogeneity in response between replicates, suggesting that genetic drift may explain some of the results.

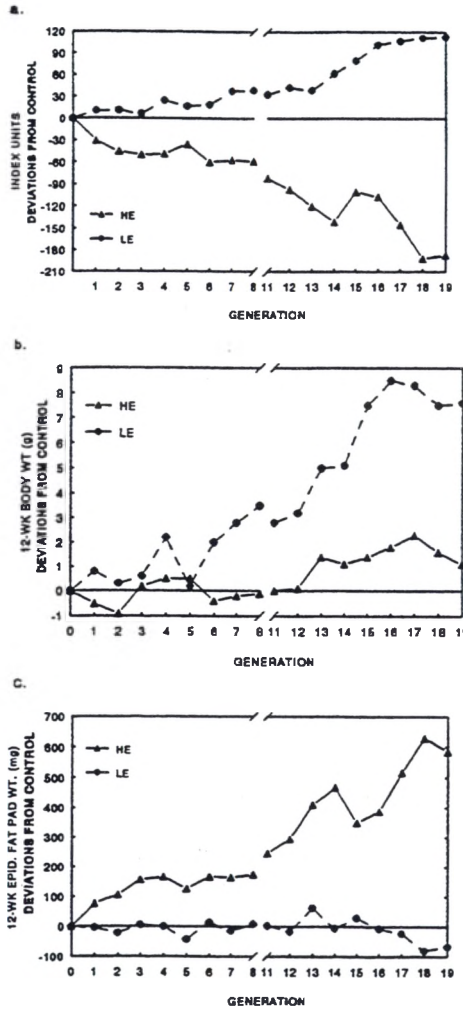


Figure 1. Generation means as deviations from control, pooled across replicates.  
 a. index units, b. 12-wk body weight, c. 12-wk epididymal fat pad weight

#### REFERENCES

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